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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,095	04/07/2005	Henry M Krause	1889-00900	5757

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EXAMINER	
SHIN, DANA H	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,095	KRAUSE ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-23* is/are pending in the application.

4a) Of the above claim(s) *1-9,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13,15-17 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on February 8, 2007.

Currently, 1-13 and 15-23 are pending. Applicants have cancelled claim 14 and added claim 23. Claims 1-9 and 18-19 have previously been withdrawn for being drawn to non-elected inventions.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

Claims 10, 12, 15-17 and 20-22 stand rejected under 35 U.S.C. 102(a) as being anticipated by Srisawat et al. (*Methods,* 26:15-161, 2002) for the reasons of record as set forth in the Office action mailed on August 8, 2006 and for the reasons stated below.

Applicant's arguments filed on February 8, 2007 have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain

features of applicant's invention, it is noted that the features upon which applicant relies (i.e., multiple palindromic restriction sites) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant further agues that the insulator sequences claimed in the instant case function to ensure proper folding of the tags and to discourage interactions between the tags and the inserted target RNA. Applicant contends that the spacers of Srisawat et al. are not workable for the purpose of ensuring proper folding of the tags and discouraging interactions between the tags and the inserted target RNA. Contrary to applicant's contention, Srisawat et al. expressly teach that one of main considerations in constructing affinity tag molecules is the folding problem. They explicitly teach that the "folding problem is "simply" a matter of inserting the tag in such a way that both the tag and the RNA of interest remain correctly folded." (page 158) Further, they state that the "steric blockage problem arises when the tag is partially or completely covered by either the folded structures of the RNA or its associated protein subunits, thus obstructing access of the tag to the affinity matrix. Therefore, if the information about the structure or accessibility of the RNA of interest is available (e.g., form RNA footprinting study), it will be very helpful in choosing the insertion site that is less likely to have the steric blockage problem." (page 159) They teach that one potential solution to the steric blockage problem is to "place a short spacer between the tag and the main body of the RNA". See page 159.

Applicant further alleges that the spacers disclosed in the Srisawat et al. reference are likely to interfere with the folding of the tags or the target RNA without providing any evidence supporting such allegation. As stated above, Srisawat et al. expressly teach that spacers are

inserted to remedy the folding and steric blockage problems (pages 158-159). Examiner does not understand the basis/premise behind applicant's allegation.

Further, the intended function of insulator elements are not claimed or recited in the instant case. Regardless, since the spacers of Srisawat et al. are capable of performing the same intended use as the instantly claimed insulator elements, all of the claim limitations are clearly taught by Srisawat et al.

Claim Rejections - 35 USC § 103

Claims 10-12, 15-17, and 20-22 remain rejected under 35 U.S.C. 103 for being unpatentable over Srisawat et al. (*Methods,* 26:15-161, 2002) in view of Rigaut et al. (*Nature Biotechnology,* 17: 1030-1032, 1999) for the reasons of record as set forth in the Office action mailed on August 8, 2006 and for the reasons stated below.

Applicant's arguments filed on February 8, 2007 have been fully considered but they are not persuasive. Applicant argues that one of ordinary skill in the art could not have known how to achieve the specific constructs of the current invention. Contrary to applicant's argument, the primary reference, Srisawat et al. already taught the specific constructs of the current invention. See above for reasons.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., achievement of the desired level of purity) are not recited in the rejected claim(s). Regardless, one of ordinary skill in the art would have known how to achieve the specific constructs based on the teachings of Srisawat et al., because they expressly teach that it is necessary to generate and test several tagged RNA constructs to ensure their ability to bind to the affinity matrix. In other words, since

the necessity to test various tagged RNA constructs was known in the art, one of ordinary skill in the art would have been sufficiently motivated to test a number of different tagged RNA constructs and would have succeeded in making a specific tagged RNA construct through routine optimization experimentation.

Applicant further argues that only one of the two tags of Srisawat et al. worked and that this outcome emphasizes the importance of applicant's invention, which provides tag selection and tag orientation, placement and separation, which allow both tags to function. As stated above for §102 rejection, Srisawat et al. teach tagged RNA constructs that are claimed in the instant case. The issue of how many of the RNA constructs worked is irrelevant in the instant case because it is not recited in the rejected claims. Similarly, applicant's arguments regarding the specificity of tags and ligands are not persuasive because the alleged feature is not recited in the rejected claims.

To reiterate, since the importance of testing specificity of RNA tags was already taught by Srisawat et al. it would have been obvious to one of ordinary skill in the art to design and make an RNA fusion molecule that is specific for its intended ligand and the skilled artisan would have arrived at the RNA fusion molecule through routine optimization experimentation.

Claims 10, 12-13, 15-17, and 20-22 remain rejected under 35 U.S.C. 103 for being unpatentable over Srisawat et al. (*Methods,* 26:15-161, 2002) in view of Johansson et al. (*PNAS,* 95:9244-9249, 1998) for the reasons of record as set forth in the Office action mailed on August 8, 2006 and for the reasons stated below.

Applicant's arguments filed on February 8, 2007 have been fully considered but they are not persuasive. Applicant argues that since neither Srisawat et al. nor Johansson et al. teach or

suggest the insulator sequence, as defined by applicants, the rejected claims are non-obvious over Srisawat et al. in view of Johansson et al.

First, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., insulated sequence defined by applicants: multiple palindromic restriction sites) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As stated above for §102 rejection, Srisawat et al. teach that one potential solution to the steric blockage problem is to "place a short spacer between the tag and the main body of the RNA". See page 159. Accordingly, since Srisawat et al. teach and suggest the spacer sequence that is functionally equivalent to the insulated sequence of the instant case, the rejected claims are obvious over Srisawat et al. in view of Johansson et al.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 102

Claims 10-13, 15-17, and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srisawat et al. (*Methods,* 2002, 26:15-161) in view of Bachler et al. (*RNA,* 1999, 5:1509-1516) and Bardwell et al. (*Nucleic Acids Research,* 1990, 18: 6587-6594) and Boniface et al. (US 2005/0118646 A1). This rejection is necessitated by amendments entered in the claims.

Claims 11-13, 15-17, and 20-23 depend from an amended independent claim, claim 10. Therefore, claims 11-13, 15-17, and 20-22 are considered amended by dependency from claim

10. Claim 23 is a newly entered claim. The claims are drawn to an RNA fusion molecule comprising a target RNA sequence, at least one insulator sequence, and at least two different RNA tags and at least one RNA tag is repeated.

Srisawat et al. teach a fusion RNA molecule comprising two different RNA tags, S1 and D8. They teach that one potential solution to the steric blockage problem is to "place a short spacer between the tag and the main body of the RNA". See page 159. They teach that several factors need to be taken into consideration in designing the RNA tag fusion molecule: availability of the potential affinity resins, ability to elute bound RNA without co-eluting nonspecific contaminants, and ability to have a high affinity only for specific RNAs and RNPs (page 157). Further, they teach advantages as well as disadvantages of D8 and S1 RNA tags in Table 1. Srisawat et al. do not teach repeated RNA tags nor MS2 tag.

Bachler et al. teach an RNA fusion molecule comprising Streptotag and MS2 (pages 1509-1514; Figure 1). They teach the bifunctional "MS2(wt)-apt RNA" compirising the streptomycin-binding aptamer and the wild type hairpin structure taken from the MS2 replicase mRNA interacting with MS2-CP (page 1315). They teach that their RNA fusion molecule is useful for affinity-purification method for the isolation of specific RNA-binding proteins.

Bardwell et al. teach affinity RNA tag purification method for RNA-protein complexes. They teach that an RNA containing two tandem RNA tags (two R17 recognition sites adjacent to each other) has stronger affinity to target coat protein matrix than that containing only one RNA tag (pages 6590-6591, 6593-6594; Figures 3-4).

Boniface et al. teach affinity tag purification system is useful for isolating interacting proteins or fragments (paragraphs 0002, 0007). They teach that a spacer (e.g., short peptide) can be inserted in the affinity tag purification system and that one of ordinary skill in the art can add

and optimize spacer amino acid sequences between any of the contiguous functional segments or between the bait protein and the peptide tail to allow efficient formation of multi-protein complexes and affinity purification (paragraph 0008).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the presently claimed fusion RNA molecule comprising a target RNA sequence, at least one insulated sequence, and at least two RNA tags. One of ordinary skill in the art would have been motivated to modify the structure of RNA fusion molecules of Srisawat et al. in view of the teachings of the combined prior art, because Srisawat et al. expressly teach major factors to consider with regard to the specificity of RNA affinity tags (pages 157 and 159). One of ordinary skill in the art would have had a reasonable expectation of success in modifying the RNA fusion molecules of Srisawat et al. to arrive at the instantly claimed RNA fusion molecule because the use of Streptotag and MS2 in RNA affinity purification system was already taught by Bachler et al. and because placing two identical RNA tags in tandem orientation was known to be more efficient as evidenced by the teachings of Bardwell et al. Further, one of ordinary skill in the art would have been motivated to include an insulator sequence (spacer sequence) in the RNA fusion molecule for affinity purification, with a reasonable expectation of success, because Srisawat et al. teach that one potential solution to the steric blockage problem is to place a short spacer between the tag and the main body of the RNA (page 159) and because Boniface et al. teach that one of ordinary skill in the art can add and optimize spacer sequences between any of the contiguous functional segments to allow efficient formation of multi-protein complexes and affinity purification (paragraph 0008). Accordingly, the instantly claimed invention taken as a whole would have been *prima facie* obvious at the time the invention was made.

Conclusion

No claim is allowed.

This application contains claims 1-9 and 18-19, drawn to inventions nonelected without traverse in the reply filed on June 26, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

TC1600

JANE ZARA, PH.D.
PRIMARY EXAMINER